IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of:

GEORGE M. HALOW

Serial No: **10/194,251**

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Group Art Unit: **1616**

Examiner: **Choi, Frank I**

For : **BOWEL CLEANSING COMPOSITION**

AFFIDAVIT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, George M. Halow, attest that:

I am the sole inventor of the invention described and claimed in U.S. patent application Serial No. 10/194,291.

I reside at 4305 Okeefe Drive, El Paso, Texas 79902.

I received my undergraduate degree from the University of Texas in 1970, and my degree as a Doctor of Medicine from New York Medical College in 1976. I interned and did my residency in internal medicine at Yale University from 1976 to 1979, and took my Fellowship in gastroenterology at the University of Pennsylvania from 1979 to 1981. I was subsequently awarded a Fellowship in Nutritional Science from 1981 to 1982 at The University of Pittsburgh. I have now been a practicing gastroenterologist for over 22 years.

In the course of my practice, I have personally conducted at least 20,000 colonoscopies requiring the use of a bowel cleanser (also commonly referred to as a purgative). I have attended closely to the efficacy of these cleansers, as a thorough cleansing of the bowel is critical to examination of the colon for polyps or other signs indicating a possible pathological condition.

From the beginning of my practice, I prescribed a sodium phosphate bowel cleansing composition, usually in liquid form, such as Fleet PHOSPHO-SODA, a trademark of C.B. Fleet Co., Inc., Lynchburg, VA. I have also prescribed polyethylene glycol (PEG)/electrolyte compositions, such as GOLYTELY, a trademark of Braintree Laboratories, Braintree, MA. Each of these compositions has been associated over the course of the years with a significant amount of patient non-compliance, evidenced by a poorly cleansed bowel. I estimate that at least 10 to 15% of the colonoscopies I performed using one or the other of these compositions as bowel preps had to be repeated for this reason.

On discussing this matter with my bowel cleansing patients, I have been repeatedly told that:

1) the sodium phosphate compositions were highly unpalatable; while for many the regimen was tolerable, the non-compliant patients and a significant number of compliant patients consistently reported wretching, nausea, vomiting, and an inability to comply with the regimen as instructed;

2) the PEG/electrolyte compositions were very unpleasant to ingest, owing primarily to the large volume of liquid required to accompany them; while for most it was tolerable, the non-compliant patients and a significant number of the compliant patients reported great discomfort, particularly from abdominal pain as well as bloating and nausea.

It has been apparent to me for many years that the key to bowel preparation for colonoscopy is patient compliance with the cleansing regimen, which in turn is dependent upon properties of the chosen purgative independent of its ability to cleanse the

bowel. As the most-used commercially available cleansers will typically cleanse the bowel if used by the patient in the amounts and formulations directed by their manufacturers, patient non-compliance, as evidenced by finding an only partially-cleansed bowel during the colonoscopy, is readily identified. Since this means the colonoscopy cannot be relied upon to find or predict a pathological condition, a second procedure must be prescribed. Often, the non-compliance is repeated. Too often, the patient refuses to undergo another colonoscopy. At best, the discomfort and expense of the procedure is increased for the patient. At worst, a pre-cancerous condition or localized cancer is not discovered early enough and becomes an inoperative cancer.

I started to consider how a patient-friendly bowel prep composition might be formulated. After conducting clinical studies on patients using various compositions, I determined that the bowel cleansing compositions I formulated as set forth in U.S. patent application Serial No. 09/194,291 were effective bowel cleansers and, importantly, also exhibited significantly reduced side effects, particularly bloating, nausea, vomiting, and abdominal pain. The taste was also unobjectionable to nearly all patients. Results of these clinical studies are set forth in the Application under "EXAMPLES", and also attached hereto and made a part hereof.

The Comparison Studies submitted herewith were all conducted by me in the course of my practice. These case histories include reported side-effects and palatability of the commercially-available bowel cleansers Fleet PHOSPHO-SODA and GOLYTELY when each is used alone. In my professional opinion, the effectiveness of the compositions according to U.S. Patent application Serial No. 10/194,291 far exceeded the effectiveness of either of the GOLYTELY or PHOSPHO-SODA compositions according to the prior art. I did not expect such an improvement in patient acceptance while maintaining bowel cleansing efficacy.

CASE STUDIES ACCORDING TO THE INVENTION

Methods and Materials:

Patients were prepared for colonoscopy with a dry prep composition of 60 grams PEG powder and 18 grams disodium phosphate powder per dose.

Each patent was given two single-dose packets for self-administration on the day preceding the colonscopy, with instructions to dissolve each dose in water and drink the first dose at 10 a.m. and the second at 4 p.m. For each patient, a clear liquid diet was prescribed for that day. A flavor packet containing powdered Crystal Light® Ice Tea was provided for use as desired with the prep to encourage drinking.

Results:

The results reported here are representative of those obtained in the experimental group.

Patient #1:

This is a 61 year-old female with weight loss and decrease in appetite. She underwent a clear liquid diet the day before with bowel prep taken at 10 a.m. and at 4 p.m. Good prep and adequate view of the colon was verified by multiple photographs during colonoscopy. She had no complaints of cramping or complaints of nausea. Mild dislike of taste.
View of transverse colon, Figure 1.

Patient #2:

This is an 86 year-old female with a history of anemia who underwent bowel prep, taking it twice the day before examination with a clear liquid diet. There was adequate clean out and a good view of the entire colon with no abnormalities found in the colon.

View of sigmoid colon, Figure 2.

Patient #3:

This is a 62 year-old male with hemorrhoidal bleed and diarrhea undergoing colonoscopy. Bowel prep at 10 a.m. and 4 p.m. and a clear liquid diet were prescribed. He had no complaints of nausea, vomiting, or discomfort. No complaints of taste abnormalities. He was given flavor packet to use as needed.

View of transverse colon, Figure 3.

Patient #4:

This is a 74 year-old male with a history of colon polyps for surveillance colonoscopy, underwent bowel prep and clean out the day before using the dry prop at 10 a.m. and 4 p.m. with one Dulcolax 10 milligram tablet. Adequate clean out showing diverticulosis at the sigmoid colon. Mild rectal irritation and inflammation with a good view of the entire colon verified by video photographs taken during colonscopy. Tolerance of the prep and slight complaint about taste, but no crampy sensation. No nausea and vomiting that he has had with other preps.

View of descending colon, Figure 4.

Patient #5:

This is a 50 year-old female with a first degree relative with colon cancer who underwent surveillance colonoscopy. Took the bowel prep at 10 a.m. and 4 p.m.; some stool found in the sigmoid colon. There was no liquid, able to suction out completely and got a good visualization of the entire colon verified by video photographs during he colonoscopy with the patient having no complaints of product tolerance. No nausea and no vomiting with diarrhea, and no crampy sensation.
View of transverse colon, Figure 5.

Patient #6:

This is a 50 year-old female who presented with diarrhea for colonscopy. The bowel prep was taken at 10 a.m. and 4 p.m. on the day before the exam, with a clear liquid diet. The bowel prep was good, with adequate view of colon. No complaints.
View of transverse colon, Figure 6.

COMPARISON STUDIES

In the following studies, the commercial Fleet PHOSPHO-SODA and GOLYTELY bowel cleansers were administered according to the manufacturers instructions.

Case Study I

The patient is a 57-year-old male with a family history of colon polyps. The physical examination was normal. The patient was prepped for colon examination with Fleet PHOSPHO-SODA. The day before the examination while prepping, the patient developed severe nausea, vomiting, and sharp abdominal pain. So, the patient went to the emergency room and was given IV hydration which controlled the pain. A colonoscopy was delayed because of the side effects and performed later with multiple polyps removed. They were benign.

Case Study II

This patient is a 75-year-old female presenting with six months history of intermittent abdominal pain, left lower quadrant pain, and change in her bowel pattern with increased constipation associated with bowel urgency and incomplete evacuation. Physical examination was normal except for mild-to-moderate lower abdominal discomfort with normal rectal examination. The patient was scheduled for colonoscopy and prepped PHOSPHO-SODA. During the day of the prep, the patient exhibited nausea, vomiting, and worsening of her sharp abdominal pain. Examination was delayed. Colonoscopy was done two days later with an extensive diverticulosis found in the left colon.

Case Study III

This is a 23-year-old male presenting with frequent bowel movements, up to five per day consisting of small bowel movements with bowel urgency and incomplete evacuation. No fever

or chills. No weight loss. Episodes of moderate sharp abdominal pain. This is generalized. Vital signs were normal on physical examination. Abdominal finding shows slight discomfort with variations. No abdominal guarding. Rectal exam is normal. Colonoscopy scheduled with Fleet PHOSPHO-SODA prep. The patient complained of abdominal sharp pains after taking the prep, and he went to the emergency room for evaluation, was given hydration with pain control and sent home. Colonoscopy was done two days later. Normal examination. Diagnosed with irritable bowel with diarrhea.

Case Study IV

The patient is a 72-year-old female with a history of lower GI bleeding. She was admitted to the hospital with a hemoglobin 8.7. Bleeding was noted on physical examination. Tagged RBC, radio nucleotide study showed positive point of bleeding in the left lower quadrant, with colonoscopy requested to determine the cause of bleeding. The prep was given: GOLYTELY dissolved in one gallon of water, with 8 ounces to be drunk every 10 minutes. Gallon was drunk over an hour to an hour and a half. The nausea was so severe that the patient could not tolerate the prep; her stomach was very upset with severe pain and nausea. The patient's examination was delayed today because of the side effects, rehydration given, and pain control with eventual colonoscopy was done showing findings of the sigmoid diverticular bleeding.

Case Study V

The patient is a 68-year-old male admitted to the hospital with left lower quadrant pain, decreased appetite from four months; decrease bowel function progressive for over the period of a month, with symptoms worsening. The patient admitted weight loss of about 7 to 10 pounds. On physical examination findings of left lower quadrant discomfort and slight guarding

with no evidence of surgical abdominal findings. Rectal examination unremarkable. Prep for colonoscopy requested by family practice physician was GOLYTELY at 8 ounces every 10 minutes; a total of GOLYTELY of one gallon over an hour. The patient developed severe nausea and vomiting, and unable to keep the prep down. He states that he could not tolerate the prep, it was a terrible taste with severe, sharp abdominal pain. CT scan was done, with a suspected tumor in the splenic flexure. Colonoscopy later done showed the positive diagnosis adenocarcinoma of the bowel, with the patient ending with surgical resection.

Case Study VI

The patient is a 36-year-old female with long-standing history of constipation. Bowel movements are one day per week associated with bloating. Physical examination, vital signs are stable. The examination was normal except for a slight fullness in the lower abdominal area. Her prep for colonoscopy was Fleet PHOSPHO-SODA. On the day of the prep, after taking the prep, she had severe abdominal sharp pain and abdominal bloating. She went to the emergency room, and was released after seven hours. The colonoscopy was delayed two days. The patient was then prepped with a PEG/phosphate formula according to U.S. patent application S.N. 10/194,291. The prep was completed without abdominal pain. No complaints. Colon examination was normal. Diagnosis of irritable bowel with constipation.

Case Study VII

The patient is a 63-year-old female seen for colonoscopy. She had a history of colon polyps, which were removed three years ago after colonoscopy, with severe nausea and vomiting from the Fleet PHOSPHO-SODA prep. Fleet PHOSPHO-SODA was again used as prep here, and colonoscopy performed. Patient states she would not take the prep again.

Case Study VIII

This is an 80-year old female with a history of heme positive stools. No gastrointestinal symptoms at all. Blood count is now normal. Physical examination is completely normal. Colon prep, Fleet PHOSPHO-SODA given. Nausea and vomiting, severe sharp pain and consequent delay of the examination. Patient re-prepped with another product using the solution **(WHAT SOLUTION??)**. The patient's colonoscopy was performed, and diverticulosis was found with no evidence of bleeding.

Case Study IX

The patent is a 56-year-old male with lower GI bleeding, bright red perirectum, and history of diarrhea, intermittent bleeding for a month associated with fever. Admitted by Family Practice doctor with physical examination, elevated pulse and decreased blood pressure because of dehydration. Generalized abdominal pain with guarding and rebound on abdominal examination. Laboratory data showed an evidence of elevated white count suggestive of infection. The patient was treated with IV antibiotics with clinical improvement after four days and given the GOLYTELY prep [standard instructions] for colonoscopy. He states it had a very bad taste and forced himself to take it, developing sharp abdominal pain with associated nausea. After completing the prep, he stated it was a horrible prep. He then underwent colonoscopy with the diagnosis of ulcerative colitis, possibly related to infection.

Case Study X

A 16-year-old male presenting with a history of depression and decreased bowel function. Symptoms of decreased bowel function, one bowel movement per week or every week and half. Physical examination was normal except for fullness in the lower abdominal area. Rectal deferred because it was refused by the patient. The patient's abdominal x-rays shows bowel full of

stool. The GOLYTELY prep was given for a clean out. Patient was unable to tolerate the product because of the taste and severe nausea. The patient eventually was cleaned out with enemas. He underwent a colonoscopy, and underwent a psychiatric consultation.

Case Study XI

This is a 55-year-old male who was seen for evaluation of colon screening, given GOLYTELY 8 ounces every 10 minutes the day prior to the examination, one gallon total. Nausea, vomiting developing during the prep. The patient has canceled the prep and rescheduled it because of the nausea. The colon examination was done and it was normal. The patient states that he will never take the GOLYTELY product again because of severe side effects and its bad taste.

Case Study XII

The patient is a 67-year-old male from the Veteran's Clinic sent for colon screen. History of high blood pressure, under treatment and controlled. GOLYTELY has been given by the VA Clinic as a prep, with severe nausea and vomiting throughout the night. Presented to the clinic for colonoscopy with low blood pressure, dehydration and given IV hydration before his colonoscopy. The exam was performed with several small polyps and polypectomy performed. The patient had severe complaints about the side effects of nausea and severe abdominal pain. He said he would refuse to take the prep again for another colon exam and requested other preps.

AFFIDAVIT 12

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Respectfully submitted,

George M. Halow

Attorney's Docket: A-8051.Affidavit/cat